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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/653,794	09/01/2000	Meir S. Sacks	286262-00005	5973

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ALAN G. TOWNER
PIETRAGALLO, BOSICK & GORDON
ONE OXFORD CENTRE
301 GRANT STREET 38TH FLOOR
Pittsburgh, PA 15219

EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 01/28/2004

20

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/653,794

Applicant(s)

SACKS ET AL.

Examiner

Gollamudi S Kishore, PhD

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 26-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

The request for the extension of time and amendment filed on 10-6-03 are acknowledged.

Claims included in the prosecution are 1-25.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement as set forth below. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to how to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d, 1400 (Fed.Cir.1988). Among these factors are: (1) the nature of the invention; 2) the state of the prior art; 3) the relative skill of those in the art; 4) the predictability or unpredictability of the art; 5) the breadth of the claims; 6) the amount of direction or guidance presented; 7) the presence or absence of working examples; and 8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

1) The nature of the invention: the invention concerns with the treatment of male erectile dysfunction using L-arginine or its derivatives and an antioxidant.

2) The state of the prior art: the teachings of the prior art, as pointed out by applicants themselves (their arguments on page 6 of their response, with regard to the 103 rejection based on Snyder) appear to indicate the contradictory effects of arginine and its derivatives. To summarize, according to applicants, snyder uses arginine to treat painful prolonged erections and not to treat males having erection problems (i.e., arginine makes the penis placid which is the opposite of the claimed effect).

3) The relative skill of those in the art: the skill of one of ordinary skill in the art is high (PhD level technology).

4) The predictability or unpredictability in the art: as pointed out above and based on applicant's own response, the effect of arginine and its derivatives does not appear to be predictable. Instant claims 2-5 and 14-17 recite esters of arginine which according to Snyder are NO synthase inhibitors and have an opposite effect.

5). The breadth of the claims: instant claims are broad in terms of the compounds falling within the term 'derivative' of arginine and 'antioxidant'.

6) The amount of direction of guidance provided: instant specification provides no guidance as to the effect observed in male patients.

7) The presence or absence of working examples: there are no working examples for the treatment of male erectile dysfunction using the claimed combination.

8) The quantity of experimentation necessary: since no guidance is provided as to the effectiveness of the combination of several compounds falling within the definition of

'arginine derivatives' and 'antioxidants' one of ordinary skill in the art will not be able to practice the invention without undue experimentation.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-6, 8-18 and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fossel (6,207,713) or Wallace (6,476,037) in view of Chobanian et al (6,139,847) of record.

Fossel discloses topical delivery of L-arginine (nitric oxide inducer and vasodilator) or the treatment of erectile dysfunction (note abstract, Example 3 and claims).

Similarly, Wallace discloses the topical administration of L-arginine for the treatment of erectile dysfunction (abstract, col. 15, line 53 et seq., Examples and claims).

Chobanian et al while disclosing a treatment of fibrosis teach that antioxidants such as ascorbate, tocopherol and beta-carotene are NO catabolism inhibitors and advocates the use of the combination of NO stimulators (L-arginine) and NO catabolism inhibitors (note the abstract, col. 3, line 6 through col. 4, line 67, col. 5, line 40, Example

1 and claims). Chobanian further teaches the knowledge in the art of the use of NO donors for the treatment of conditions including impotence (col. 3, lines 6-10).

The inclusion of an antioxidant in the L-arginine containing compositions of Fossel or Wallace for the treatment of erectile dysfunction would have been obvious to one of ordinary skill in the art, with the expectation of obtaining at least an additive effect, since Chobanian teaches that antioxidants are NO catabolism inhibitors and that they could be used in combination with NO stimulators. Although neither Fossel nor Wallace teach the use of the composition for female sexual dysfunction by topical application to the clitoris, it would have been obvious to one of ordinary skill in the art to use the composition for females with a reasonable expectation of success since clitoris is supplied with blood vessels and the principle of vasodilatation is the same.

5. Claims 13-18 and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fossel or Wallace in view of Chobanian et al as set forth above, further in view of Duckett et al (6007,824) by itself or in further combination with Wyson (6,031,002)

The teachings of Fossel, Wallace and Chobanian have been discussed above. As pointed out above, what are lacking in Fossel, Wallace and Chobanian are the teachings of the applicability of the arginine derivatives for the treatment of female sexual dysfunction.

Duckett et al as discussed before, disclose compositions containing L-arginine and ginseng (antioxidant) for the treatment female sexual dysfunction. Duckett et al teach that the sexual stimulation causes local release of NO resulting in the smooth muscle relaxation and the increased blood flow. They further teach that L-arginine releases NO resulting in smooth muscle relaxation and increased inflow of blood (note

the abstract, col. 1, line 12 through col. 2, line 46, col. 3, line 65 through col. 4, line 50 and claims). The mode of administration in Duckett however, is oral and not topical.

Wysor as discussed before, while disclosing prostaglandin (vasodilator) formulations for enhancing female sexual response teaches that the formulations can be applied topically to the genitals and such a topical treatment is highly effective. Wysor further teaches the use of liposome formulations for the delivery of the composition (note the abstract, columns 1-3 and claims).

In essence, the reference of Duckett shows that the principle of NO release and the increased blood flow in females by the vasodilator, arginine and that of Wysor shows that a vasodilator can be applied topically the genitals to treat female sexual dysfunction.

One of ordinary skill in the art would be motivated further to use the composition of arginine and the antioxidants of Fossel, Wallace and Chobanian to treat the female dysfunction since the effectiveness of arginine against female dysfunction and that of Wysor shows that a vasodilator composition can be applied topically to the female genitals to achieve the desired goal.

6. Claims 7 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fossel, Wallace in view of Chobanian et al (6,139,847) as set forth above, OR Fossel, Wallace in view of Chobanian et al (6,139,847) further in view of Duckett et al (6007,824) by itself or in combination with Wyson (6,031,002) as set forth above, further in view of Quan (6,180,133).

The teaching of Fossel, Wallace, Chobanian, Duckett, and Wysor has been discussed above. What is lacking in these references is the use of ascorbyl palmitate.

Quan while disclosing topical antioxidant formulations teaches that ascorbyl palmitate is stable and due to its fat solubility, it penetrates the skin more readily than

ascorbic acid reaching comparatively high levels in much shorter periods of time (note col. 5, lines 45-55).

The use of ascorbyl palmitate or ascorbyl palmitate in combination with ascorbic acid would have been obvious to one of ordinary skill in the art since ester form is fat soluble and penetrates the skin more readily as taught by Quan. The use of a mixture would have been obvious since such a use would achieve both rapid slow response times.

Applicant's arguments have been fully considered, but are deemed to be moot in view of these new rejections.

The reference of Duckett (6,340,480), which teaches topical application of arginine, is cited of interest.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is 703 308 2440. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703 308 2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.



Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK